Polarization vision and the development of retinal network models

Neuronal information transfer functions from cones and horizontal cells to bipolar cells

Final report

Maarten Kamermans (PI)
Craig Hawryshyn (Co-Pi)

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14. ABSTRACT

This report results from a contract tasking The Netherlands Ophthalmic Research Institute as follows: The final study demonstrated how cones compress natural stimuli into a dynamic range the rest of the visual system can cope with. Furthermore, the study demonstrated how horizontal cells, that store global stimulus parameters such as spectral composition and e-vector orientation of the global stimulus, adjust the gains of the cone synapse such that it suits the global stimulus conditions. It was also found that bipolar cells process these responses and how interaction between inputs to bipolar cells enhances their sensitivity to changes of intensity, color and presumably e-vector orientation. We identified an additional level of gain control in bipolar cells. Finally additional opponent processing of horizontal cells could not be revealed at the ganglion cell level. This indicates that just as in the spectral domain, opponency in horizontal cells is an efficient way of information coding and does not reflect a critical analysis step in 3-vector processing. Horizontal cell system is the memory of the global spectral composition and e-vector orientation of the animal.

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General outline of the project

The visual system has an extraordinary processing capability. Often the vertebrate visual system surpasses man-made imaging devices in flexibility and performance. Using knowledge of retinal physiology and retinal information transfer schemes will lead to the development of very flexible and high performance imaging devices. The overall objective of the program is to move towards the development of polarization chip technology for use in imaging devices in autonomous vehicles performing under extreme optical conditions.

To fulfill this aim, a collaboration was started between Dr. Craig Hawryshyn, an expert in polarization vision and Dr. Maarten Kamermans, an expert in retinal circuitry. This team examined the information transfer function and the retinal processing of polarization information, in order to develop mathematical models of polarization vision. The experiments dealing with polarization vision were conducted in Kingston (Canada), while those regarding the transfer functions from photoreceptors to horizontal cells and bipolar cells were performed in Amsterdam (The Netherlands). Figures 1 and 2 give the general scheme of the project which was funded as follows:

Project 1: Polarization sensitivity of horizontal cells (Kingston). Funded by an AFOSR grant to Hawryshyn (PI) and Kamermans (CoPI).

Project 2: Photoreceptor to horizontal and bipolar cell neuronal communication (Amsterdam). Funded by this EOARD grant to Kamermans (PI) and Hawryshyn (CoPI).

This report describes mainly the part funded by the EOARD. However, to illustrate the progress made in the whole project, it also incorporates data generated in the part funded by the AFOSR. These experiments will be inferred to as such when applicable.

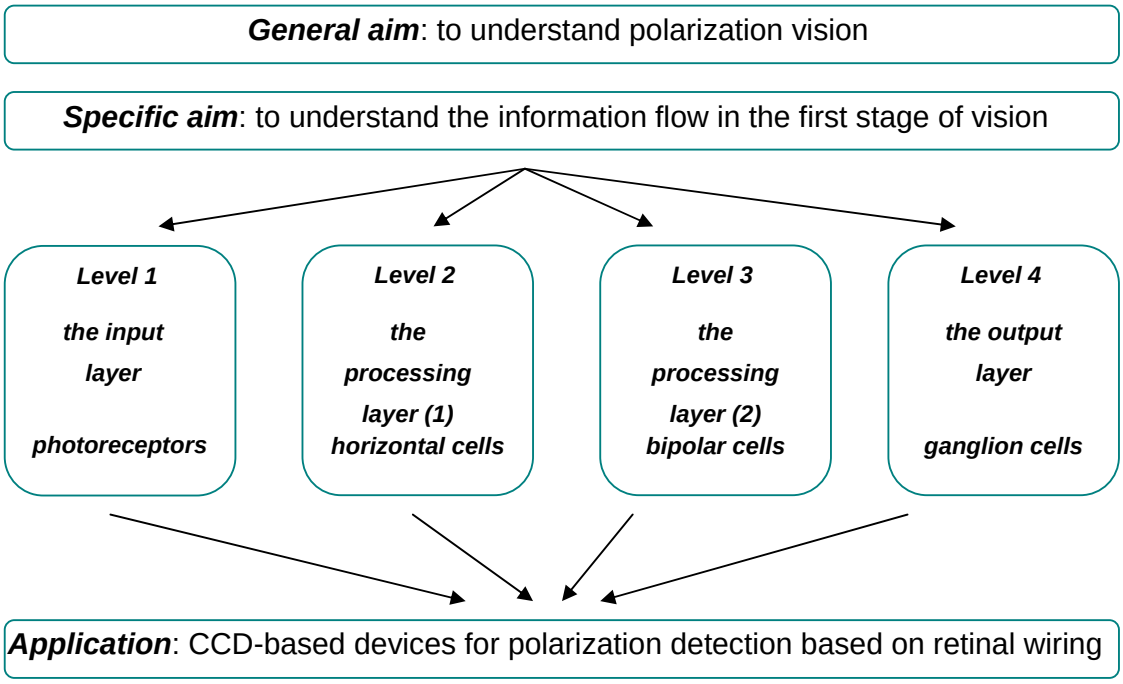

Figure 1. General scheme of the project

Specific aims

Level 1 - The input layer – photoreceptors

The generation of a quantitative model of photoreceptors under natural stimulus conditions

Level 2: - The processing layer (1) - horizontal cells

Description of the influence for horizontal cells on the synaptic activity of cones.

Comparison of spectral and e-vector tuning of horizontal cells

Level 3: - The processing layer (2) - bipolar cells

Description of properties and interaction of photoreceptor inputs in bipolar cells

Description of gain control mechanism in bipolar cells

Level 4 - The output layer - ganglion cells

Estimate e-vectors processing in the outer retina versus inner retina

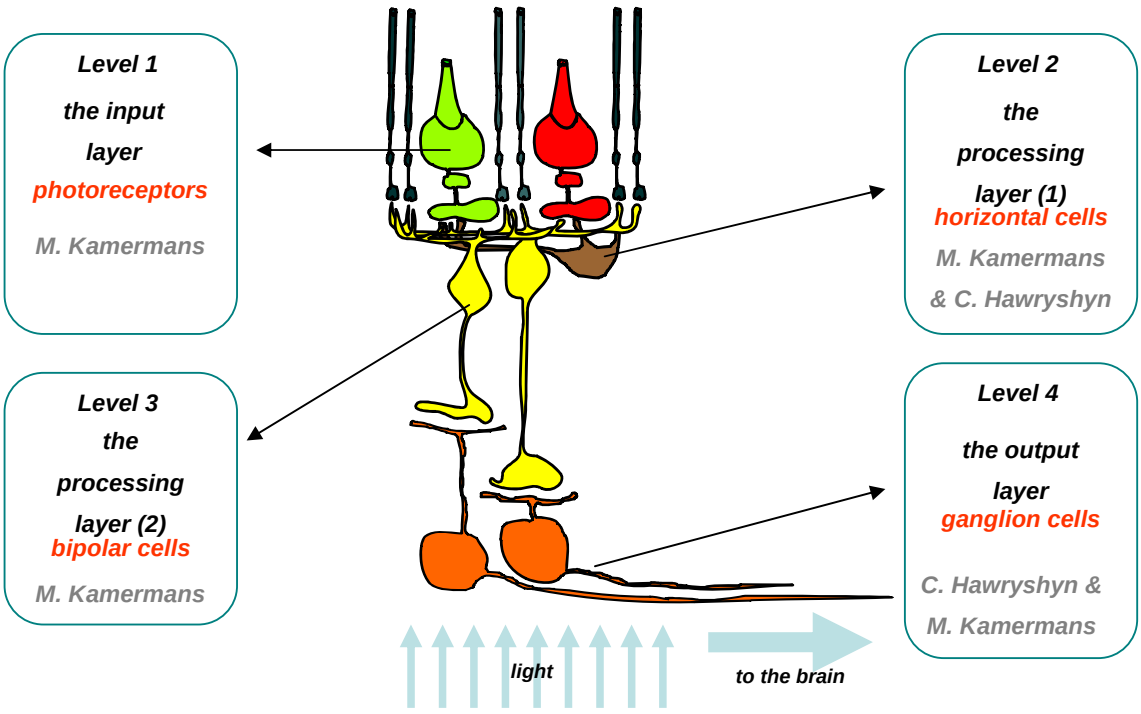

Figure 2. Various levels of research

Obtained results

Level 1 - The input layer - photoreceptors

Visual stimuli as encountered by animals in natural scenes are very different from random stimuli. They display strong correlations in space, time and wavelength (van Hateren, 1993), and often encompass a large range of intensities and contrasts. Much of the processing in the early stages of visual processing, in particular those in the retina, is concerned with reducing these correlations and compressing the intensity and contrast ranges such that they fit the limited dynamic range of neurons. An important goal of visual neuroscience is to understand the mechanisms by which decorrelation and dynamic range reduction are accomplished, and how these influence visual perception. Before these issues can be studied, the spectral sensitivity of cones needs to be determined.

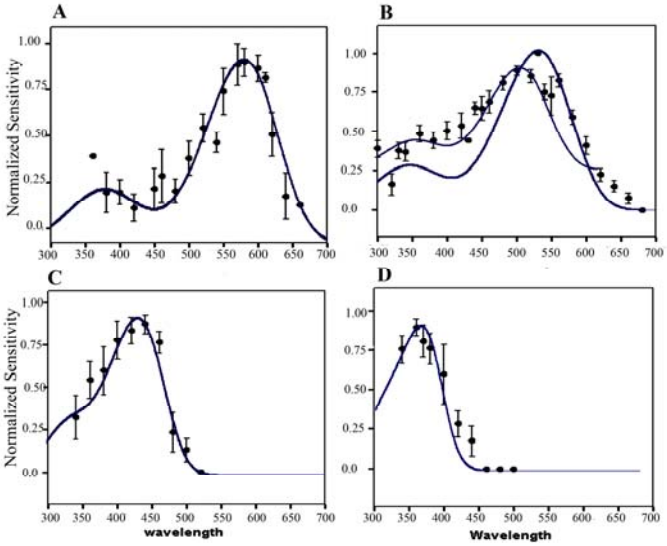

Figure 3 Spectral sensitivity plots of salmon cones. Data points represent action spectra and solid lines indicate absorption spectra.

Spectral sensitivity of cones

In this study a number of fish species were used; goldfish, salmon and zebrafish. The spectral sensitivity of cone in goldfish has been determined before (Kraaij et al…..). For salmon and

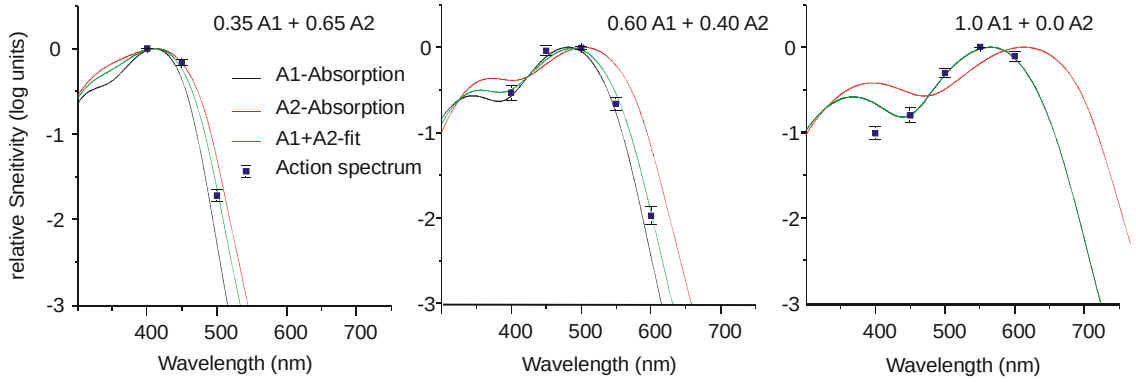

Figure 4 Spectral sensitivity of zebrafish cones. Data points represent action spectra and solid lines indicate absorption spectra.

zebrafish these were never determined directly. The salmon data were collected by the group of Hawryshyn and the zebrafish data by the group of Kamermans. Figure 3 shows the spectral sensitivity plots for the zebrafish cones and Figure 4 shows similar plots for the salmon cones.

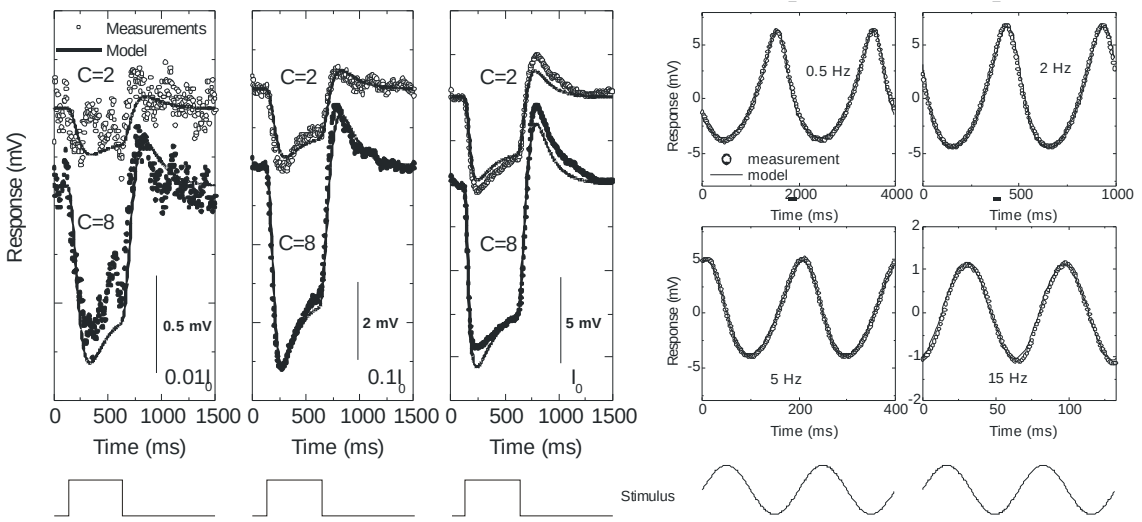

Figure 4. Horizontal cell responses to steps and sinosoids of light for different contrasts. Frequency of the sinosoids ranged from 0.5 to 15 Hz. The solid line in the data figure is the response of the model.

Cone compression

First we concentrated on the initial step in visual processing, which takes place in the cone photoreceptors of the vertebrate retina. In particular, we were interested how natural stimuli are processed, and if the critical physiological steps involved herewith could be identified and understood. We used goldfish cones as our model system, because it is possible to obtain good and stable measurements from these cells. Cones were characterized using steps of light and sinusoids of light of different frequencies. Figure 3 shows cone responses to such stimuli. These data are used to tune a model of the photoreceptor (Figure 4). The solid lines in Figure 3 are the model responses to the stimuli. Note that the model captures the non-linear distortions of the responses accurately. See for instance the responses to the sinusoids. The responses deviate markedly from a pure sine wave. Although it is often assumed that the early steps in visual processing are essentially linear (See for instance: Vu et al., 1997), we show here that such an assumption is not correct for natural stimuli. The high dynamic range of such stimuli causes the cone to display marked nonlinearities, and a nonlinear model is necessary to adequately describe its responses. We adapted the Van Hateren model (van Hateren, 2005; van Hateren & Snippe, 2007) for the cones and could show that the observed

nonlinearities can be fully understood from what is known on the phototransduction system in cones. These results show that one needs a nonlinear model to adequately describe cone light responses.

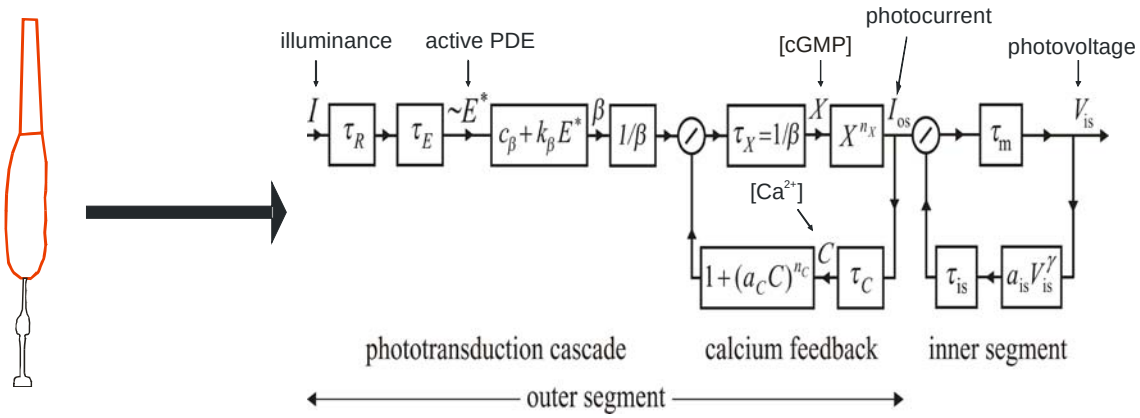

Figure 5. Photoreceptor model. Modified from Van Harteren et al., (2005).

In this part of the study, we used highly artificial stimuli. Since we are interested in the behavior of the retina under natural conditions, we switched to natural stimuli. We used a natural time series of intensities (NTS) recorded outdoors, which contains a high dynamic range, a wide temporal frequency bandwidth, and considerable temporal correlations. Figure

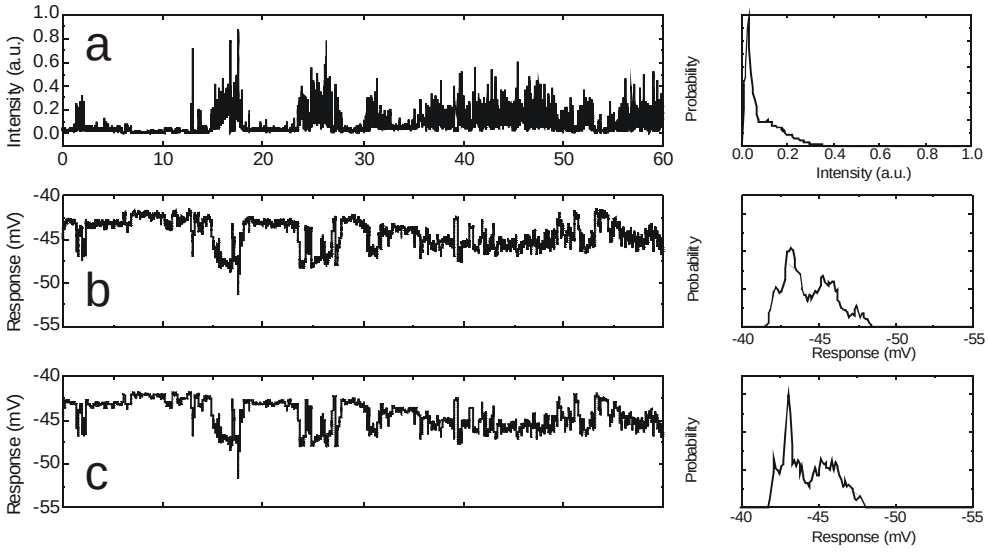

Figure 6 Cones compress visual information. Left: a natural time series of intensities or NTS (a), and responses of a goldfish cone (b) and of our vertebrate photoreceptor model (c) to the same NTS. Right: probability density functions of the NTS (a), of the cone responses (b) and of the model responses (c). Cones compress the peaks and troughs of the NTS, transforming the highly skewed distribution of the natural scene (a) into a more balanced one (b). Note that the model responses (c) reproduce very accurately the compression performed by the cones.

5a shows the distribution of intensities in a natural scene (left panel) and the probability density function, i.e. the distribution of intensities (right panel). Low intensities are highly present in natural scenes: the distribution of intensities is highly skewed towards low intensities with a long shoulder at the high intensity side. Figure 5b shows the responses of a cone when stimulated with the stimulus depicted in Fig 5a (left), as well as the distribution of the cone response amplitudes. This graph is very different than the one in figure 5a: cone response amplitudes are nicely positioned around the mean membrane potential of -45 mV. This means that cones have compressed the natural stimulus in order to make optimal use of their limited dynamic range preventing thereby saturation. Figure 5c shows the model response to the NTS. The model captures the responses of cones with an accuracy of about 95%. Such high accuracy indicates that the model responses to natural stimuli are not statistically different from the physiological responses.

Analysis of the model parameters showed that goldfish and primate cones (including human cones) perform in a remarkably similar way, the major difference being the response dynamics. These dynamic variations, in turn, can be completely accounted for by temperature differences between goldfish and primates.

A paper of this work is in preparation.

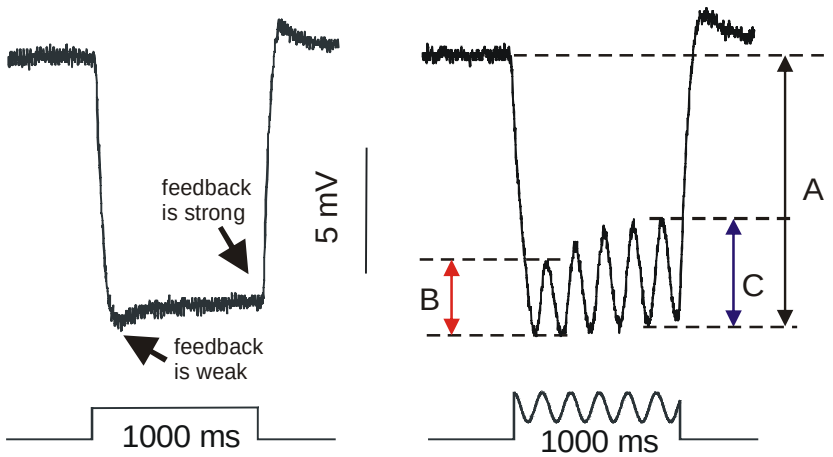

Figure 7. Light response of a horizontal cell due a step steady (left) or sinwave modulated (right) of light. Feedback is hardly present in the earlier part of the response and becomes pronounced in the later part of the response. The response to the sinewave component of the stimulus is smaller in the earlier part of the response (arrow b) compared to the later part of the response (arrow c) indicating that the synaptic gain increases with feedback strength.

Level 2: - The processing layer (1) - horizontal cells

After the compression performed by the photoreceptors, the visual signal has to pass the cone/horizontal/bipolar cell synapse. What modifications of the signal occur at this stage?

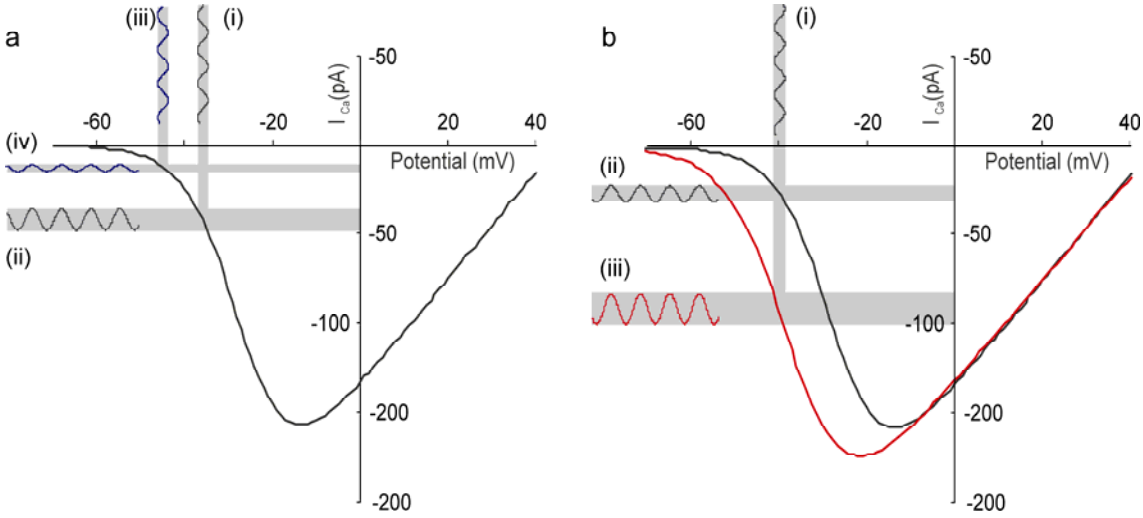

Figure 7. The proposed mechanism. a) A schematic representation of the Ca-current of a cone. If one modulates the membrane potential of the cone a few mV around -35 mV (i) a relatively large modulation of the Ca-current occurs (ii). When the cone membrane potential is modulated at more hyperpolarized potentials (-45 mV) (iii), the resulting modulation of the Ca-current is much smaller (iv). b) A schematic representation of the Ca-current without feedback (black line) and with feedback (red line) from horizontal cells. The modulation of the cone membrane potential by a few mV around -40 mV (i) leads to a smaller modulation of the Ca-current when horizontal cells are at their resting membrane potential (ii) compared to the condition when horizontal cells are hyperpolarized (iii).

Gain control at the horizontal cell synapse

The gain of this synapse in not static, but strongly depends on the horizontal cell activity. Since such gain changes in the first synapse of the visual system might have great impact on the visual performance of the whole animal, we studied the mechanism responsible for these gain changes in detail. We started to determine the relation between the cone membrane potential and the output of the cone.

By measuring responses of cones and horizontal cells in conditions in which horizontal cell activity was modified, we could show that horizontal cell hyperpolarization generates a negative feedback signal to the cones. This signal has a complex nature; it has a multiplicative and a subtractive component. The subtractive component is the most studied one. Here we focused on the multiplicative component since we believe that this component is the most important component when considering natural stimulus conditions. We could

show that horizontal cell hyperpolarization leads to an increase of the synaptic gain as explained below.

Figure 6 shows the response of a horizontal cell to a flash of sinusoidally modulated light. Early in the response, the sine-wave stimulus generates a sinusoidal response with small amplitude. The amplitude of this response increases with time. We showed that this change in gain is due to the modulation of the Ca^{2+}-current of the cones by horizontal cells. This is the negative feedback mechanism we have previously described (Verweij et al., 1996; Kamermans et al., 2001). Finally a model has been developed which adequately describes this behavior (Figure 7)

The implications of these results are far reaching. To understand how the gain modulation in the outer retina affects the output of the retina as a whole, we have to consider the relation between cone and horizontal cell responses and the ganglion cell responses. When doing so, it becomes clear that the sustained response component of cones and horizontal cells is not transmitted to ganglion cells with high fidelity since most ganglion cells respond with transient responses (Figure 8). Even "sustained" ganglion cells have a strong transient component. This means that the subtractive part of negative feedback is mostly lost while the multiplicative part remains prominently present when considering the effect horizontal cells have on ganglion cell responses: i.e. the output of the retina. The gain modulation affects the responses of the ganglion cell and thus the rest of the visual system strongly.

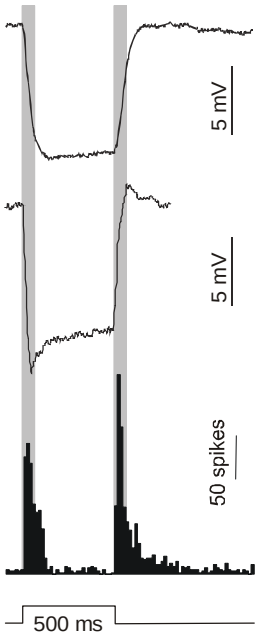

Figure 8. Light response of a cone, Horizontal cell and ganglion cell to the same stimulus. The sustained part of the light response of cones and horizontal cells is not transmitted to ganglion cells.

Most of the visual processing depends on the measurements of a local parameter (center) and a spatial (or spectral) average of the same parameter (surround). The cones measure the local properties of the stimulus and horizontal cells measure the global properties of the stimulus.

Direct stimulation of a cone leads to a gain reduction whereas activation of the horizontal cells leads to a gain increase. This means that when considering natural stimuli, horizontal cells are not inhibiting the center but activation of horizontal cells actually *enhances* the sensitivity of center. In other words, horizontal cells measure the global stimulus parameter and adjust the gain of the cone output accordingly. Such an adjustment might be an essential component of a color constancy system (Kamermans et al., 1998; VanLeeuwen et al., 2007).

A paper about this topic is submitted

e-vector sensitivity of horizontal cells

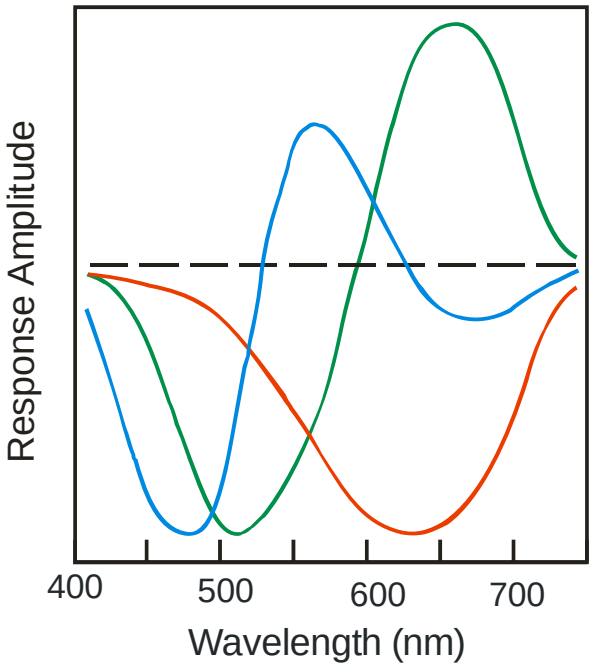

Figure 9. Spectral sensitivity of horizontal cells in the goldfish retina. (red: monophasic horizontal cell; green: biphasic horizontal cell; blue: triphasic horizontal cell)

A similar arrangement is to be expected for polarization vision. One could imagine that horizontal cells will transmit in one way or the other the information about the general e-vector orientation (surround) whereas the cones will transmit the local orientation (center). The bipolar cells would thus contain the information about the e-vector orientation relative to the general e-vector orientation. This kind of organization as been described in the spectral domain; fish and reptile, horizontal cells are spectrally coded. One can distinguish mono, bi and triphasic horizontal cells in these animals. Monophasic horizontal cells hyperpolarize over the whole visible spectrum, biphasic horizontal cells hyperpolarize in the blue-green range of the spectrum and depolarize in the red part of the spectrum and triphasic horizontal cells hyperpolarize in the blue and the red part of the spectrum and depolarize in the green part of the spectrum (Figure 9). Although horizontal cells are spectrally coded, their output to the cones is not. When measured at the cone level, this feedback signal is no no longer opponent (Kraaij et al., 1996). We concluded that the feedback signal is a weighed sum of the activity of the horizontal cells. That raised the question why horizontal cells were spectral coded. We hypothesized that the spectral coding of horizontal cells is a very effective way of storing the spectral information, since opponent coding removes redundant information (Buchsbaum & Gottschalk, 1983; Kamermans et al., 1998; VanLeeuwen et al., 2007). In other words horizontal cells store the spectral information of the scene in a highly effective way. Do horizontal cells use opponent coding to process e-vector information as well?

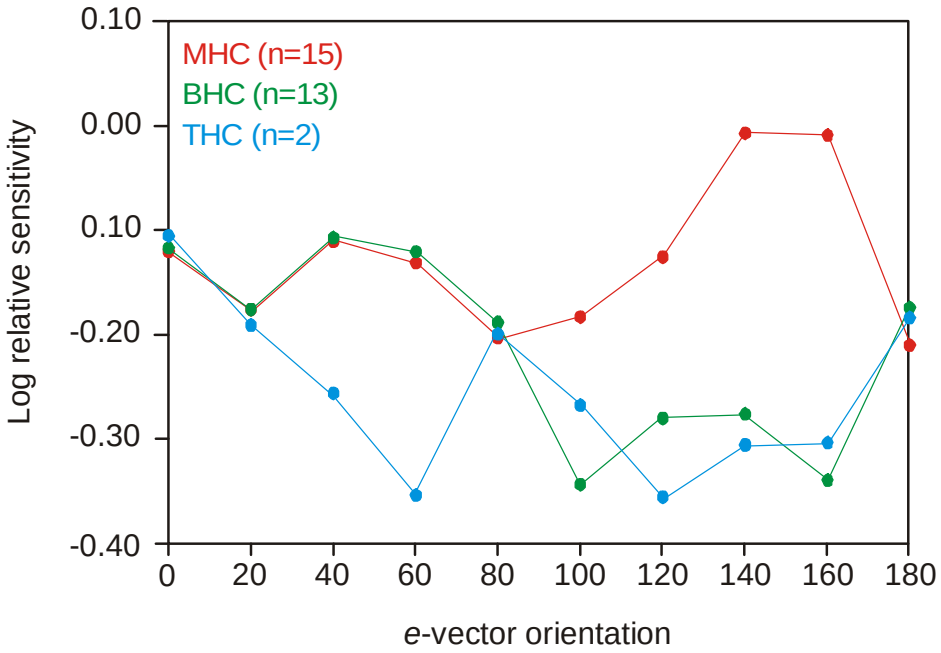

Figure 10. E-vector tuning of goldfish horizontal cells (data collected in Kingston).

It is highly likely that similar processing occurs in the e-vector domain. If this is the case one expects that at least two types of horizontal cells exist: one that sums the two orientations and at least one that takes the difference between the two orientations. Together these two horizontal cell types would be able to generate a feedback signal to the cones that contains information about the mean e-vector. This part of the project has been addressed in the Hawryshyn lab in Kingston and will yield a precise description of the relation between e-vector of the light stimulus and the horizontal cell activity. These experiments were part of the AFOSR-funded part of the project and will be reported on extensively by Dr. Hawryshyn. In short, using intracellular recoding techniques, three types of horizontal cells could be distinguished (Figure 10) as far as their e-vector tuning curves are concerned.

Although the e-vectors tuning differs from the spectral tuning, the global resemblance of both coding schemes is striking. It suggests that, apart from storing the global spectral information, the horizontal cell system also stores information about the global e-vector orientation. We hypothesize that, again, the opponency found at this level only indicates a way of effective information coding and does not reflect an essential processing step for color or e-vector processing. We will come back to this point later in this report. The experiments dealing with the e-vector processing are presently studied in more depth by the group of Hawryshyn in Kingston.

Level 3: - The processing layer (2) - bipolar cells

Since bipolar cells transmit the information of the outer retina to the inner retina, analyzing the activity of the bipolar cells is essential to understand the total output of the retina. Especially knowledge about the transfer functions between the various neurons in the outer retina is crucial for any device one wants to build based on retinal neurophysiology. We therefore studied the relation between horizontal cell and photoreceptor activity and bipolar cell responses next. These experiments were performed in goldfish since these fish are widely used for retinal research, have UV cones and well-characterized neurophysiologically properties. The retinal slice preparation was chosen because it is the only one in which the synaptic transfer functions can be determined properly.

Interaction of Photoreceptor Inputs in Bipolar Cells

At many levels in the retina, visual information is split into two main pathways as a means of computing data optimally. Horizontal cells, bipolar cells and ganglion cells all use a broadband channel and at least one opponent channel to transmit information about color, contrast and movement to the forthcoming neurons. It seems natural to suppose, therefore, that polarization vision may also be subserved by the same coding scheme.

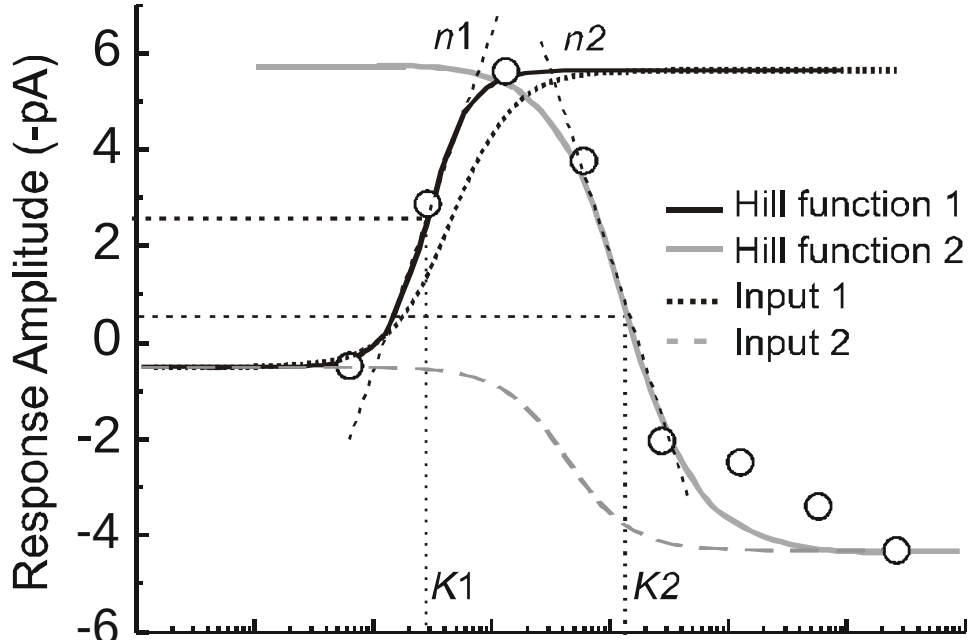

Figure 11. Intensity–response curves of an opponent mixed-input bipolar cell (continuous lines) and of its inputs (dashed and dotted lines) to the same kind of light stimulation. In the mesopic range, this mixed-input bipolar cell type is more sensitive to changes in light intensity than either of its inputs. This bipolar cell is therefore a very effective intensity change detector.

To understand the computational power of such a scheme, we studied the origin and function of spectral opponency in bipolar cells. We described this type of organization at the bipolar cell level, showing that opponency in goldfish mixed input bipolar cells can be generated by either interactions between rods and cones, or by interactions between spectrally distinct types of cones. Our analysis indicated that these cells, previously thought to underlie color vision only, are much more suited to detect intensity changes (Figure 11). This increased sensitivity to changes appears because the antagonistic inputs render the intensity-response relation of these cells much steeper than that of a single photoreceptor type; small intensity changes lead, as a consequence, to large response changes. This part of the work has been published.

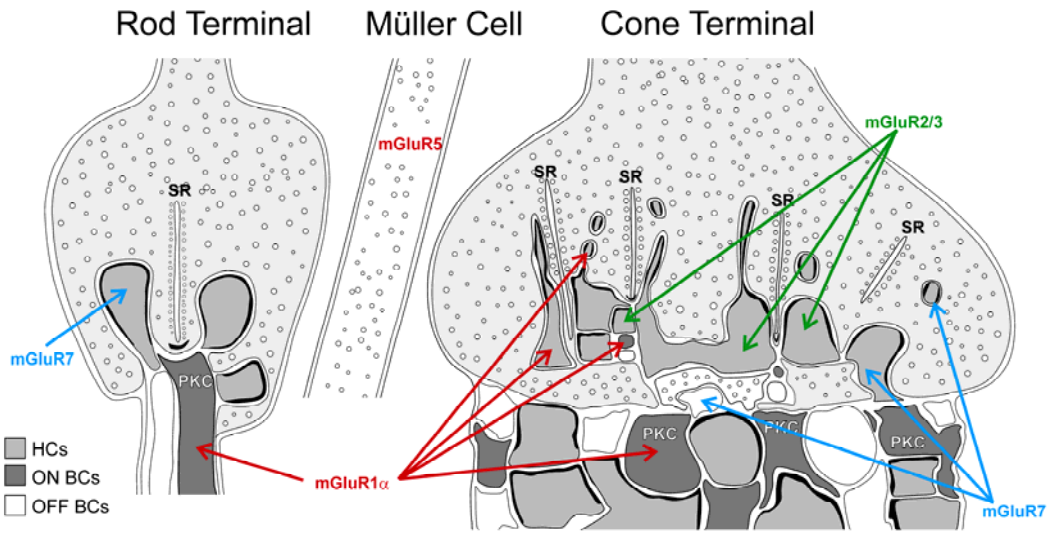

Figure 12. Schematic drawing of the distribution of mGluRs in the synaptic terminal of rods (left) and cones (right). Contrary to the generally accepted view that only mGluR6 is involved in the signal transmission between photoreceptors and second order neurons, we find a myriad of different mGluRs in the outer plexiform layer. These receptors will most likely be involved in shaping the dynamics of the horizontal and bipolar cell responses under various adaptation conditions.

Study of the mGluR Composition at the First Synapse

Glutamate is the neurotransmitter used by photoreceptors to communicate with second-order neurons. In order to understand the formation of the opponent and non-opponent channels that subserve color, contrast, motion and polarization vision, it is therefore fundamental to know the glutamate receptor makeup of retinal neurons, and how these receptors contribute to light responses. We performed a light- and electron microscopy study of the metabotropic glutamate receptor (mGluR) localization in the outer plexiform layer of the goldfish retina.

Double-labeling experiments with the ON bipolar cell markers PKCα and Goα were carried out in order to determine which mGluRs are present at the dendrites of these cells. Processes of putative mixed-input ON bipolar cells in this synapse are also positively labeled for mGluR1α, whose function remains obscure: all rod-driven ON bipolar cell responses are abolished by group III agonists in goldfish.

Surprisingly, mGluRs of all three groups were localized to horizontal cell dendrites. The function of these mGluRs at the horizontal cell level is unknown. They might be involved in shaping light responses, since the light-driven conductance in horizontal cells is mediated by AMPA/KA receptors. Müller cells, the retinal glia responsible for glutamate uptake, expressed mGluR5. Figure 12 shows a summary diagram of the results. We performed some pharmacological experiments to investigate this hypothesis. The localization of the mGluR's has been published.

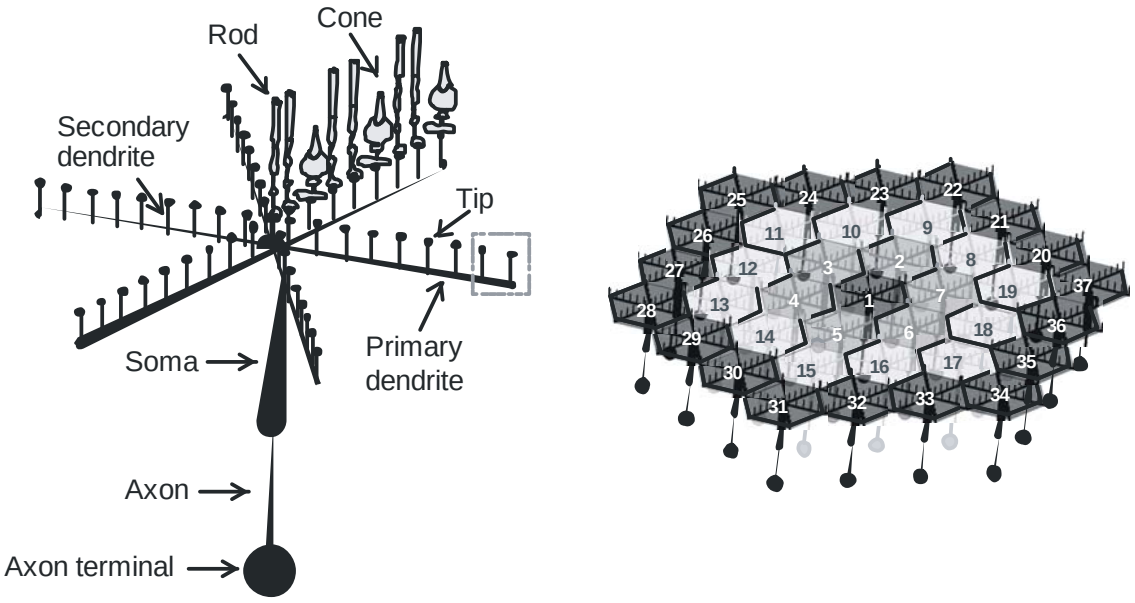

Figure 13. Model of the mixed-input bipolar cell network. Mixed-input bipolar cells contact both rods and cones (b). Therefore, they have to perform well both in photopic as well as in scotopic conditions. To facilitate this, a gain control mechanism is present at the tips of the bipolar cell dendrites (b). The diameter of the secondary dendrite and the presence of voltage-gated K^+ channels in the tips of the dendrites are the essential components of such a mechanism. This mechanism allows the bipolar cell and its coupled neighbors (c) to optimally respond in a very large intensity range.

Gain Control Mechanisms in Mixed-Input ON bipolar cells

Mixed-input ON bipolar cells of the fish retina respond to light via two different mechanisms, a conductance decrease with a negative reversal potential driven by cones and a conductance increase with a positive reversal potential driven by rods. The multiplicity and the

characteristics of the photoreceptor inputs to mixed-input ON bipolar cells generate a big paradox at the first synapse. Due to their opposing conductance mechanisms, rod- and cone-driven pathways might shunt the one another. To function optimally in both the dark-adapted, rod-dominated state, and in the light-adapted, cone-dominated state, mixed-input bipolar cells need to have special mechanisms to adjust the gain of the rod-bipolar cell synapse at different light levels. The presence of voltage-gated currents at the tips of the dendrites of mixed-input ON bipolar cells turns out to be very important for the gain modulation of mixed input bipolar cells. Because of these voltage-gated (probably K^+) channels, light responses rectify at positive potentials in voltage-clamp experiments. We elaborated a model using NEURON to investigate the interaction between K^+ currents and rod-driven light responses (Figure 13). Simulations indicate that the dendritic localization is crucial for the dynamics of the light responses and for the rectification of *IV* relations, suggesting a role for these conductances in modulating the gain of the rod-bipolar cell synapse (Figure 14). In the scotopic range, they

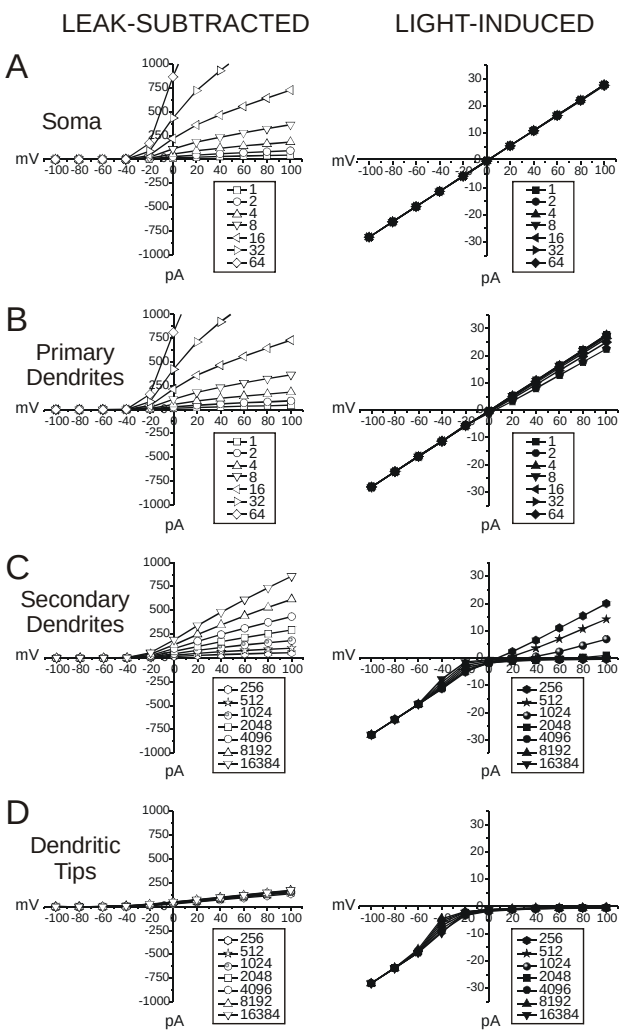

Figure 14: The effect of compartmentalization of K+ channels on light-induced (rod-driven) *IV* relations. A) K^+ channels confined to the soma; B) K^+ channels confined to the primary dendrites; C) K^+ channels confined to the secondary dendrites; D) K^+ channels confined to the tips of the secondary dendrites. Left panels (open symbols) depict leak-subtracted whole-cell *IV* relations for increasing K^+ channel densities (values in pS/µm2 at the bottom of the graphs). Right panels (closed symbols) show the light-induced *IV* relations in each condition for all values of I_{KV}. Somatic (A) and dendritic (B) K^+ channels do not contribute to the rectification of light-induced currents. Only when the voltage-gated K^+ channels are restricted to the secondary dendrites (C) or to the tips of the secondary dendrites (D) rectification is achieved. The largest amount of rectification is observed when voltage-gated K^+ channels are concentrated at the tips of the dendrites, in the vicinity of the mGluR6-driven channels. In this condition, light-driven *IV* relations rectify considerably even when the leak-subtracted currents are very small.

speed up synaptic transmission and generate transience by directly interfering with light responses. This fast repolarization could restore the high gain of the rod-bipolar cell synapse, allowing subsequent rod-driven signals to drive the cell efficiently. As light levels increase, tonic suppression of the rod input would lead to the opening of many voltage-gated channels, shunting the rod pathway and decreasing the gain of the rod-bipolar cell synapse. We are currently preparing a manuscript about these results.

Parallel processing in the fish retina

At the bipolar cell level, many processing channels are generated. This divergence of the visual signal into parallel streams is common to all vertebrate species, albeit the number and type of channels may vary. One interesting question is why one needs to process visual information in parallel. Another interesting question is how parallel, that is, how independent, these retinal channels really are. Lastly, one wonders whether the structural variations found in different animals classes change the function of individual retinal subsystems, that is, whether one can or cannot directly compare inner retinal processing in lower vertebrates such as the goldfish with that of higher primates. We wrote a paper in which we discuss these topics in depth. The manuscript was submitted to *Vision Research* and is presently under review.

Level 4 – the output layer – ganglion cells

Ganglion cells form the output stage of the retina. Any signal that is sent to the brain has to pass these neurons. Responses of ganglion cells (compound action potentials - CAP) can be reliably recorded in the optic nerve and are therefore often used as a first estimate of the activity of the retina. Another measure for retinal activity is the electro retinogram (ERG) measurements. These measurements estimate the mean activity of the outer retina. Comparing these two measurements (CAP and ERG) will indicate the type of transformation the retinal circuit performs. Therefore, we studied the dependence of the CAP and ERG on the e-vector of the stimulus light. These experiments were performed in the AFOSR part of the project and will be described in the AFOSR report in detail. A short summary is given below.

To evaluate the output of the retina in the e-vector domain we studied the CAP measured in the optic nerve. These measurements indicate a strong retinal contribution to the processing of polarized light. The CAP recordings showed a W-shaped sensitivity curve, with a peak a 0°, 90° and 180°, consistent with processes for both vertical and horizontal orientation

(Figure 15). Next we compared the e-vector tuning of the CAP recordings with the e-vector tuning of the ERG recordings. Such comparison might enable the separation of outer and inner retinal mechanisms for e-vector processing. In the ERG, in addition to the peaks at 0°, 90° and 180°, two additional peaks appeared at 45° and 135°. This result suggests a specialized contribution of outer retinal in processing of polarized light.

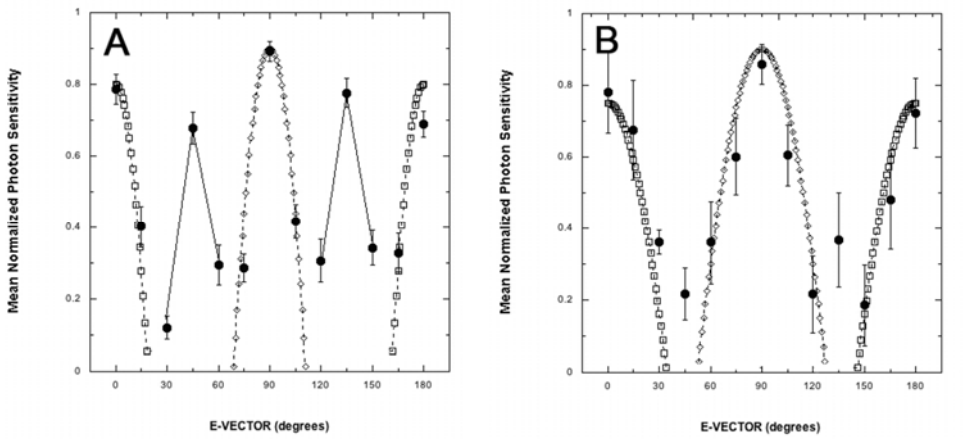

Figure 15. e-vector tuning of the ERG (left) and CAP (right). Both the ERG and the CAP show pronounced peaks at 0º, 90º and 180º. The ERG shows additional peaks around 45º and 135º indicating additional local coding in the outer retina (data collected in Kingston).

In addition, a pharmacological approach was used to determine the underlying neurophysiological basis. Opponent processing can occur via negative feedback or by opponent feedforward inputs. Both of such interactions occur at the cone/horizontal/bipolar cell level. The effect of blocking negative feedback from horizontal cells to cones on the ERG was studied by injecting low doses of cobalt in the eye. A low dose of cobalt is known to block this feedback pathway. It was found that the intermediate peaks reduced after application of cobalt suggesting that these peaks are due to outer retinal inhibition.

A simple computational model was developed to evaluate these results. The model consists of opponent and non-opponent processing elements for the two polarization detectors. This model provides a first approximation analysis suggesting that additional opponent coding occurs in the outer retina. The finding that this coding is lost at the output level of the retina strongly suggests that the opponent processing in the outer retina is related to optimal coding. These results are consistent with the idea that horizontal cells store the average information about the spectral composition and e-vector orientation of the whole scene.

A paper about these results is in press.

General Conclusion

In this study we have shown how cones compress natural stimuli into a dynamic range the rest of the visual system can cope with. Furthermore, we have shown how horizontal cells, that store global stimulus parameters such as spectral composition and e-vector orientation of the global stimulus, adjust the gains of the cone synapse such that it suits the global stimulus conditions. Next we showed how bipolar cells process these responses and how interaction between inputs to bipolar cells enhances their sensitivity to changes of intensity, color and presumably e-vector orientation. We identified an additional level of gain control in bipolar cells. Finally we showed that, additional opponent e-vector processing by horizontal cells can be measured in the ERG. The finding that this additional opponent processing of horizontal cells can not be revealed at the ganglion cell level indicates that, just as in the spectral domain, opponency in horizontal cells is an efficient way of information coding and does not reflect a critical analysis step in e-vector processing. Horizontal cell system is the memory for the global spectral composition and e-vector orientation of the animal.

Collaboration

The collaboration between the Hawryshyn lab and the Kamermans lab has been very stimulating. Technical approaches only available in the Kamermans lab before the start of the project can now be routinely be used in the Hawryshyn lab. Hawryshyn with his students and Kamermans have visited each others labs on a number of occasions. These visits have been instrumental for the technical experience transfer. Furthermore, regular discussions about research results either by email or by phone contact have influenced the ideas in both labs. The concepts now studied would not have been developed if the labs had worked independently on these issues.

Future research

Although a lot of progress has been made, many issues related to polarization vision still remain to be elucidated. Recently genetically modified fish that lack feedback from horizontal cells to cones have been generated in the Kamermans lab. These fish are a very valuable asset to study polarization vision in vertebrates. No other animal system is at present available to study polarization vision without outer retina inhibition. Future research will include at least the following topics:

- E-vector sensitivity of retinal neurons. Measure the spectral, dynamic and e-vector properties of cones, HCs, BCs, GCs and the feedback signal from HCs to cones using natural stimuli.
- E-vector sensitivity of retinal neurons under compromised HC feedback on cones. Measure the spectral, dynamic and e-vector properties of cones, HCs, BCs, GCs and the feedback signal from HCs in cones using natural stimuli in animals with a compromised feedback pathway from HCs to cones.
- Behavioral testing of e-vector discrimination under conditions that HC to cone feedback is compromised. We will compare the e-vector discrimination capabilities of wild type and connexin-mutated zebrafish behaviorally.
- Quantitative model for retinal e-vector processing. The generation of a quantitative model accounting for retinal e-vector processing. This model will be based on retinal circuitry and tries to stay as closely to the physiology as feasible. Such model will indicate the crucial coding steps for e-vector discrimination.

Output

Published papers

- S. Ramsden, L. Anderson, M. Mussi, T. Haimberger, M. Kamermans, C. Hawryshyn (2008) Retinal processing and opponent mechanisms mediating ultraviolet polarization sensitivity in rainbow trout (Oncorhynchus mykiss) *J. Exp. Biol.* (In press)
- Joselevitch, C.; Klooster, J.; Kamermans, M. (2007) Localization of metabotropic glutamate receptors in the outer plexiform layer of the goldfish retina. *Cell & Tissue Research* 330: 389-403.
- Joselevitch, C.; Kamermans, M. (2007) Interaction between rod and cone inputs in mixed-input bipolar cells in goldfish retina. *Journal of Neuroscience Research* 85: 1579-1591.
- M. van Leeuwen, C. Joselevitch, I. Fahrenfort and M. Kamermans. (2007) The contribution of the outer retina to color constancy: a general model synthesized from primate and fish data. *Vis Neurosci* 24:1-14

Papers submitted and in preparation

- Joselevitch, C.; Kamermans, M. Where fish and mammals meet: parallel pathways and crossroads in retinal processing. (*submitted*)
- M. van Leeuwen, I. Fahrenfort, T. Sjoerdsma, R. Numan and M. Kamermans. Lateral inhibition potentiates instead of inhibits centre responses of retinal neurons. (*submitted*)
- D. Endeman, M. Kamermans, H. van Hateren Cones perform a nonlinear transformation on natural stimuli (*in preparation*)
- Joselevitch, C.; Kamermans, M. Dendritic voltage-gated potassium channels and gain control in mixed-input ON bipolar cells (*in preparation*)

- L. G. Anderson and C. W. Hawryshyn Cone photoreceptor action spectra in rainbow trout (*Oncorhynchus mykiss)* using whole-cell patch clamp recording (*in preparation*)

Abstracts

- Joselevitch, C.; Kamermans, M. Interaction between rod and cone inputs in mixed-input bipolar cells in goldfish retina. *Investigative Ophthalmology and Visual Science* 48: E-Abstract 3230/B39, 2007.
- Joselevitch, C.; Kamermans, M. Dendritic potassium channels in mixed–input ON bipolar cells. *Investigative Ophthalmology and Visual Science* 46: E-Abstract 1123, 2005.
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- Joselevitch, C.; Klooster, J.; Kamermans, M. Gain control in mixed-input ON bipolar cells. Internal Meeting of the Department of Cellular and Molecular Physiology, Yale University School of Medicine, New Haven, USA, 2008.
- M. Kamermans Gain control in the outer retina. Dag voor de Biofysica. Amsterdam, The Netherlands, 2007
- M. Kamermans The role of horizontal cells in vision. Gottingen, Germany, 2007
- M. Kamermans Inhibition in the outer retina: mechanism and function. Kingston, Canada, 2007
- M. Kamermans What do horizontal cells do? Winter Brain Conference. Snowmass, USA. 2007
- M. Kamermans The role outer retinal inhibition in vision. Basel, Switserland. 2007

- Joselevitch, C.; Klooster, J.; Kamermans, M. Gain control in mixed-input ON bipolar cells. Vision and Neuroscience Symposium of The Netherlands Institute for Neuroscience, Amsterdam, The Netherlands, 2007.
- Joselevitch, C. Transforming light into neuronal responses. Meeting of the Netherlands Neuro-Ophthalmological Society, Utrecht, The Netherlands, 2007.
- M. Kamermans A retinal mechanism for Color Constancy. Lousiville, USA. 2006
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Final statement

"The Contractor, Dr. Maarten Kamermans, hereby declares that, to the best of its knowledge and belief, the technical data delivered herewith under Contract No. FA8655-05-C-4018 is complete, accurate, and complies with all requirements of the contract."

DATE: 20 April 2008

Name and Title of Authorized Official:

Prof. Dr. M. Kamermans
Professor in the Neurophysiology
Groupleader: Retinal Signal Processing

"I certify that there were no subject inventions to declare as defined in FAR 52.227-13, during the performance of this contract."

DATE: 20 April 2008

Name and Title of Authorized Official:

Prof. Dr. M. Kamermans
Professor in the Neurophysiology
Groupleader: Retinal Signal Processing